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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,499	12/03/2004	Samuel J. Shuster	14848-007US1	4520

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EXAMINER	
MCGARRY, SEAN	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
09/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,499	SHUSTER ET AL.	
	Examiner	Art Unit	
	Sean R. McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *14 and 16-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/11/05;4/27/06;8/08/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I and the accessible regions 463-490 of SEQ ID NO:1 and 894-911 of SEQ ID NO: 2 in the reply filed on 3/24/08 is acknowledged. The traversal is on the ground(s) that the examiner is incorrect in his assertion that each antisense behaves in a different way and the each antisense does not contain a common structure that provides for its activity. This is not found persuasive because applicant has not pointed out why the examiners reasoning is wrong and furthermore it is clear from the rejections below that no common special technical feature linking the inventions has been established.

The requirement is still deemed proper and is therefore made FINAL.

Claims 14 and 16-23 and the target regions recited in claims 1 and 4 other than those specified as elected above are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3/24/08.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 recites "wherein each antisense oligonucleotide specifically hybridizes within a different accessible region" It is not clear from the context of the claim whether this limitation refers back to the accessible regions recited in claim 4 or whether they also include other non recited accessible regions.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 15 rejected under 35 U.S.C. 102(b) as being anticipated by Jian et al [Am. J. Physiol. Lung Cell Mol. Physiol., Vol.276:L1046-L1051, 2001, cited on IDS filed 4/27/06].

Jian et al disclose antisense oligonucleotides targeted to the sequence around the translation start site of each of the alpha, beta, and gamma subunits of ENaC. See abstract, page L1049 and Figure 3, for example.

Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Zucchi et al [PNAS Vol. 96(4):13766-13770, 11/23/1999, cited on IDS filed 4/27/06]].

Zucchi et al have disclosed antisense oligonucleotides targeting epithelial Na+ channel beta subunit [equivalent to ENaC beta}. See 13767, for example.

Claims 12 and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Lifton et al [US 6,551,775].

Lifton et al antisense oligonucleotides and nucleic acid constructs for the expression of antisense targeted to ENaC alpha, beta, and gamma. See column 8, 17 and 18, for example.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10, 12, 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zucchi et al [PNAS Vol. 96(4):13766-13770, 11/23/1999, cited on IDS filed 4/27/06], Jian et al [Am. J. Physiol. Lung Cell Mol. Physiol., Vol.276:L1046-L1051, 2001, cited on IDS filed 4/27/06], Lifton et al [US 6,551,775], Liang et al [WO 02/24950, cited by applicant], and Bennett [US 5998,148].

The claimed invention is as clearly set forth in the claims. No interpretation is required to apply the prior art.

The target nucleic acid sequences [SEQ ID NO: 1 and SEQ ID NO: 2] are known published rat and human ENaC beta sequences (see page 4 of the instant specification, for example).

Zucchi et al have taught the use of antisense oligonucleotides targeting rat epithelial Na+ channel beta subunit via 20mer oligodeoxynucleotide antisense molecules. Zucchi et al utilized antisense technology to determine gene function and identification of genes associated with ENaC beta biological activity. It is also taught the ENaC beta is associated with Liddle Syndrome. See abstract, pages 13767 and 13768 and 13770.

Jian et al have taught the use of antisense oligonucleotides that target rat ENaC alpha, beta, and gamma I a study of ENaC biological activity. See abstract, pages L1049 and1050, and Figure 3, for example.

Lifton et al have taught diseases associated with ENaC. It has been taught the target ENaC beta with antisense oligonucleotides and with antisense expression units, including tissue specific vectors that can be used to express antisense in vivo in cells. It is taught that antisense molecules can be used to target human ENaC beta as well as ENaC beta of animal models. It has been taught that antisense targeting ENaC beta can be used to identify biological and pathological processes mediated by ENaC, identify proteins and other genes that interact with ENaC, and Identify agents that can be exogenously supplied to overcome ENaC deficiencies, and for the use as an ENaC inhibitor in a therapy that requires a decrease in ENaC expression, for example. See columns2, 3, 5, 8, 17, and 18, for example.

The prior art has therefor shown that antisense is a regularly used tool for gene activity studies where it is clear that antisense has been used specifically to inhibit ENaC beta in such studies.

The prior art above does not teach the recited target region of the instant invention or the specified modifications to antisense oligonucleotides.

Liang et al, however teach the method used in the instant application to derive target regions for antisense. For example, at pages 8 and 23 of the instant specification it is disclosed that the method of PCT/SE01/02054 which is the application for this cited WO document. Liang et al have taught the method used in the instant application to derive targetable regions on an mRNA.

Bennett et al have taught general targeting guidelines at columns 3-4, for example. It has been taught to target 5'untranslated regions, start codons, coding regions, and 3'untranslated regions of a desired target, for example. It has been taught in column 5, for example, that antisense compounds are commonly used as research reagents and diagnostics, for example. At column 5 it has been taught that antisense oligonucleotides 8-30 nucleotides in length are particularly preferred. At columns 6-7 it has been taught preferred antisense oligonucleotides contain modified internucleoside linkages including phosphorothioate linkages, for example. At columns 7-8 it has been taught that preferred antisense oligonucleotides comprise modified sugar moieties including2'-O-methoxyethyl. It has also been taught to modify nucleobases in antisense oligonucleotides at column 8-9 which includes the teaching of 5-methyl cytosine and at column 10 it has been taught chimeric antisense oligonucleotides. All of the above

referred to modification are known in the art to provide beneficial attributes to antisense oligonucleotides such as increased hybridization and nuclease protection, for example. At columns 10-24, for example it has been taught numerous "carriers" for antisense oligonucleotides. In table I it has been taught the successful targeting of those regions taught in columns 3-4 with chimeric phosphorothioate oligonucleotides having 2'-MOE (a 2'-O-methoxyethyl modification).

The prior art has therefore shown a method, that was used by applicant, to derive targetable regions for antisense. The prior art has taught the inhibition of the targeted gene of the invention and therefore provides a clear motivation for making antisense to this gene target. The prior art also teaches the size ranges and the use of vectors in the antisense art. The instant invention amounts to the use of a known method for determining targetable regions of a mRNA where the target of the instant invention has already been shown to be targeted by antisense for gene function studies, for example.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zucchi et al [PNAS Vol. 96(4):13766-13770, 11/23/1999, cited on IDS filed 4/27/06], Jian et al [Am. J. Physiol. Lung Cell Mol. Physiol., Vol.276:L1046-L1051, 2001, cited on IDS filed 4/27/06], Lifton et al [US 6,551,775], Liang et al [WO 02/24950, cited by applicant], and Bennett [US 5998,148] as applied to claim 4 above, and further in view of Branch.

The claimed invention is as clearly set froth in the claim.

The prior art cited above teaches all of the limitations of the invention other than the limitation of requiring a composition comprising multiple antisense targeted to different regions of the same target gene [ENaC beta].

Branch et al, however, disclose that it was known in the art to enhance specificity of antisense in cells and teach that it was known in the art to deploy multiple antisense compounds, each directed against a different target site in the same target RNA and thereby achieve annihilation by molecular triangulation. See page 48, for example.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R. McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Primary Examiner
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